

Office Action Summary

Application No.

09/677,574

Applicant(s)

YANG ET AL.

Examiner

Richard G Hutson

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1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/31/2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 21-39, 41, 42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-10 and 37-40 is/are rejected.
- 7) ☐ Claim(s) 11-20 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Claims 1-42 are at issue and are present for examination.

Applicant's election without traverse of Group I, Claims 1-20 and 37-40 in Paper No. 8 is acknowledged.

The requirement is deemed proper and is therefore made FINAL.

Claims 21-36 and 41-42 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b).

Priority

Acknowledgement is made of Applicants claim to the benefit of the filing date of U.S. Provisional Application Nos. 60/056,263, filed August 29, 1997, 60/060,131, filed September 26, 1997; and 60/085,247, filed May 13, 1998. It is noted that this application is also a continuation of Application Serial No: 09/141, 522, filed 8/27/1998, now abandoned. It is suggested that applicant update the first line of the specification to reflect this information.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate

paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not identify the city and either state or foreign country of residence of each inventor. The residence information may be provided on either on an application data sheet or supplemental oath or declaration.

Claim Objections

Claims 14, 17, and 20 are objected to because of the following informalities:

Claims 14, 17, and 20 each list a number of amino acids which are to be substituted for a specific position in the O-helix of the mutant polymerase. One of the amino acids included in this list is "Try". It is believed that it is applicants intent to refer to the amino acid "Tyrosine" whose three-letter code is "Tyr" not "Try". This is supported by applicants specification on page 20, lines 5-7.

Claims 11-20 are objected to because they depend from rejected claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 4, 8, 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite in that it is drawn to the polymerase of claim 1 or 2, wherein said polymerase is a DNA or RNA polymerase. The claim is indefinite in that it is unclear what other types of polymerases the polymerase of claim 1 or 2 could be referring to such that claim 3 further limits each of these claims. Are there nucleic acid polymerases that are not either DNA or RNA polymerases?

Claim 4 is indefinite in that it is unclear in the recitation "...said polymerase is mesophilic..." It is unclear what characteristic of a polymerase would make it mesophilic? Is it applicants intent that the polymerase is obtained from a mesophilic organism, or is it only active up to some threshold temperature?

Claim 5 is indefinite in that it is unclear in its recitation of specific known polymerases and "... mutants, variants, fragments and derivatives thereof." What is the scope of the term "mutant, variant, fragments, and derivatives thereof"? When does one polymerase cease to be a mutant, variant and/or derivative of one polymerase and become a "... mutant, variant and/or derivative of a different polymerase. Expansion of this argument raises the issue that it is unclear if any or all known polymerases, both DNA, RNA and those yet to be discovered would not be considered a mutant, variant or

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derivative of one or all the polymerases listed in claim 5, such that claim 5 does not further limit claim 3.

Claim 8 is indefinite in that it is unclear as to applicants intent that the claimed polymerase is mutated to reduce or eliminate discriminatory activity. If it is applicants intent that the activity that is reduced or eliminated is "discriminatory activity against one or more dideoxynucleotides" it is suggested that the claim be amended as such.

Claim 10 is indefinite in the recitation of "the O-helix of said polymerase", as it is unclear what is considered the O-helix of said polymerase. While applicants may teach a number of such O-helices of a number of known polymerases, it is unclear what in addition to that region of the polymerase defined by SEQ ID NO: 1, would be considered to be encompassed by the O-helix of a specific polymerase.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 37-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-10 are directed to all possible nucleic acid polymerases which have been modified or mutated to increase or enhance fidelity (Claim 1), or which have been modified or mutated to reduce or eliminate misincorporation of nucleotides during

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nucleic acid synthesis (Claim 2), wherein said polymerase is a DNA or RNA polymerase (Claim 3), wherein said polymerase is mesophilic or thermostable (Claim 4), wherein said polymerase is selected from those species and mutants, variants, fragments and derivatives thereof listed in claim 5, wherein said polymerase further comprises one or more modifications or mutations to reduce or eliminate one or more activities selected from the group consisting of (a) the 3'-5' exonuclease activity of the polymerase; (b) the 5'-3' exonuclease activity of the polymerase; and (c) the discriminatory activity against one or more dideoxynucleotides (Claim 6, 7, 8, and 9), wherein said polymerase comprises one or more modifications or mutations in the O-helix of said polymerase (Claim 10). Claims 37-40 are directed to kits comprising the above claimed mutant polymerases. The specification only provides the representative species encompassed by these claims, wherein the DNA polymerase consists of a combination of the following mutations: those mutants having an increase or enhancement of fidelity, consisting of mutation of Arg⁷²² or Lys⁷²⁶. There is no disclosure of any particular structure to function/activity relationship in the claimed genus. The specification also fails to describe additional representative species of these DNA Polymerases by any identifying structural characteristics or properties other than having increased or enhanced fidelity, reduced 3' 5' exonuclease activity of the polymerase, reduced 5' 3' exonuclease activity or reduced discriminatory behavior against dideoxynucleotides for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms

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that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Barnes (U.S. Patent No. 5,436,149, issued 7/25/1995).

Barnes teach a thermostable DNA polymerase with enhanced thermostability and enhanced length and efficiency of primer extension, specifically they teach the *Thermus aquaticus* DNA polymerase mutant Klentaq-278 which has an increased fidelity thereby reducing its misincorporation of nucleotides, relative to the wildtype enzyme (column 6, lines 19-35). The DNA polymerase mutant taught by Barnes further comprises a mutation in the 5'-3' exonuclease activity of the polymerase, thus claims 1-6 and 9 are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 37-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barnes (U.S. Patent No. 5,436,149, issued 7/25/1995).

As discussed above, Barnes teach the *Thermus aquaticus* DNA polymerase mutant Klentaq-278 which has an increased fidelity thereby reducing its misincorporation of nucleotides, relative to the wildtype enzyme. Barnes further teach the use of the taught polymerase mutant in methods of amplification, DNA sequencing and mutagenesis.

One of ordinary skill in the art at the time of filing would have been motivated to combine the polymerase taught by Barnes with the additional components needed for the methods taught by Barnes including dideoxynucleoside triphosphates and deoxyribonucleoside triphosphates so that the practice of the taught methods would be made more convenient and easier. The reasonable expectation of success of the combining of the necessary components of the taught methods is high based on the high degree of knowledge in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapy Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
April 22, 2002

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PRIMARY EXAMINER
GROUP 1000
1600



A DOCPHOENIX

APPL PARTS

IMIS	_____
Internal Misc. Paper	
LET.	_____
Misc. Incoming Letter	

371P
PCT Papers in a 371Application

A...
Amendment Including Elections

ABST
Abstract

ADS
Application Data Sheet

AF/D
Affidavit or Exhibit Received

APPENDIX
Appendix

ARTIFACT
Artifact

BIB
Bib Data Sheet

CLM
Claim

COMPUTER
Computer Program Listing

CRFL
All CRF Papers for Backfile

DIST
Terminal Disclaimer Filed

DRW
Drawings

FOR
Foreign Reference

FRPR
Foreign Priority Papers

IDS
IDS Including 1449

NPL
Non-Patent Literature

OATH
Oath or Declaration

PET.
Petition

RETMAIL
Mail Returned by USPS

SEQLIST
Sequence Listing

SPEC
Specification

SPEC NO
Specification Not in English

TRNA
Transmittal New Application

CTNF
Count Non-Final

CTRS
Count Restriction

EXIN
Examiner Interview

M903
DO/EO Acceptance

M905
DO/EO Missing Requirement

4/19/02 NFDR
Formal Drawing Required

NOA
Notice of Allowance

PETDEC
Petition Decision

OUTGOING

CTMS	_____
Misc. Office Action	

1449
Signed 1449

892

ABN
Abandonment

APDEC
Board of Appeals Decision

APEA
Examiner Answer

CTAV
Count Advisory Action

CTEQ
Count Ex parte Quayle

CTFR
Count Final Rejection

INCOMING

AP.B
Appeal Brief

C.AD
Change of Address

N/AP
Notice of Appeal

PA..
Change in Power of Attorney

REM
Applicant Remarks in Amendment

XT/
Extension of Time filed separate

Internal

SRNT
Examiner Search Notes

CLMPTO
PTO Prepared Complete Claim Set

ECBOX
Evidence Copy Box Identification

WCLM
Claim Worksheet

WFEE
Fee Worksheet

File Wrapper

FWCLM
File Wrapper Claim

IIFW
File Wrapper Issue Information

SRFW
File Wrapper Search Info